

IN THE SPECIFICATION:

Please SUBSTITUTE the following replacement paragraph(s) for the corresponding paragraph(s) at the page and line numbers indicated:

*Please replace the paragraph at page 3, lines 1-7 with the following amended paragraph:*

The method of arriving at recombinant collagen-like polymer has been described in detail in ~~the previously filed copending non-prepublished patent applications EP-98204263.2 (EP-A-926543) filed on 15 December 1998, which corresponds to NL 1007908 filed on 24 December 1997, and EP 99204382.8 (EP-A-1014176), by the same applicant,~~ commonly owned USP 6,150,081, inventors van Heerde et al., for example at column 14, line 48 to column 15, line 17, at column 22, line 51 to column 25 line 18 and elsewhere throughout the specification, the content entire disclosure of which patent is herein hereby incorporated herein by reference thereto. The methodology is described in the publication 'High yield secretion of recombinant gelatins by *Pichia pastoris*', M.W.T. Werten et al., *Yeast*, 15, 1087-1096 (1999), in press.

Any of the embodiments disclosed in the ~~copending previously mentioned patent application~~ van Heerde et al. USP 6,150,081 can be applied for the oil-in-water emulsions according to the invention. A preferred embodiment of an oil-in-water emulsion according to the invention is one wherein the recombinant collagen-like polymer has an isoelectric point at least 0,5 pH units removed from the pH of the oil-in-water emulsion itself. Suitably one pH unit removed or even more. The advantage hereof is that the pH at which the emulsion needs to be maintained or used or prepared can vary depending on the isoelectric point (pI) of the applied recombinant collagen-like polymer. The recombinant technology enables variation previously unavailable for tailoring the polymer and thus tailoring the pI. It will be appreciated that not all processes requiring an oil-in-water emulsion are best carried out at pH 6 which is the pH value at which prior art gelatin comprising oil-in-water

emulsions were optimally used. Naturally the pH=6 can also be used in those cases where it is still useful or in fact optimal. However the oil-in-water emulsions according to the invention no longer need the strict control of the pH during any of the processes e.g. preparation, storage or application as was previously the case. Now it has in addition become possible to use the oil-in-water emulsions according to the invention at pH=5. It has now become possible to develop oil-in-water emulsions with recombinant collagen-like polymers of extremely divergent pI values. Suitable embodiments involve pI anywhere from 4-10. pI equal to or higher than 6, equal to or higher than 7 and even equal to or higher than 8 and higher than 9 have been achieved and they are illustrated in the examples. We also illustrate pI selected from 4-7. The presence of collagen-like polymers with an isoelectric point far from the actual pH of the OW emulsion according to the invention is preferred. Such a pH has the advantage that the overall charge and the overall three dimensional conformation of the polymer is independent of the pH, and so the steric stabilisation of the OW emulsion is also independent of the pH.

*Please replace the paragraph at page 7, lines 4-31 with the following amended paragraph:*

Due to the development of the recombinant technology it has now become possible to develop for use specifically in oil-in-water emulsion according to any of the embodiments of the emulsions according to the invention recombinant collagen-like polymer exhibiting an amphiphilic structure, with one end of the molecule being polar and the other end being apolar e.g. wherein the recombinant collagen-like polymer exhibits an amphiphilic structure, with one end of the molecule being polar due to the presence of a sufficient number of polar amino acid residues to render that end polar and the other end being apolar due to the presence of a sufficient number of apolar amino acid residues to render that end apolar. Collagen-like polymers with an amphipolar character (one side hydrophilic, one side hydrophobic) show an optimal interfacial behaviour and have a strong preference for a position on the oil-water interface (with one leg in the oil-phase and "one leg"

in the water-phase, resulting in a low interfacial tension) by which the initial size and stabilisation are optimised. The manufacture of the polar hydrophilic collagen molecule can be made following the detailed method described in ~~the copending non-prepublished European patent applications EP-A-0926543 and EP-A-1014176 by the same applicant~~ van Heerde et al. USP 6,150,081. Obviously the changes required in the amino acid sequence can be achieved in a manner well known to the skilled person when wishing to introduce a few specific amino acid substitutions. The skilled person also knows which amino acids can be substituted and which amino acids can be used to enhance polarity or apolarity. The polar and apolar constructs can be combined using standard methodologies of ligation for the manufacture of the bi-functional collagen-like polymer. Not only is an oil-in-water emulsion as such part of the invention but also any of the bipolar molecules as such and a process for making them. An amphiphilic recombinant collagen-like polymer i.e. polar at one end and apolar at the other to a degree sufficient for the polar end to extend into a water phase and the apolar end to extend into an oil phase, wherein recombinant collagen-like is further as described for any of the recombinant collagen-like polymers as components of an oil-in-water emulsion according to the invention is thus also covered.

*Please replace the paragraph at page 13, lines 19-23, with the following amended paragraph:*

The production of gelatin 1 (MW = 54kD) and gelatin 2 (MW = 28 kD), which can be used in the emulsions of the invention, is described in ~~EP-A-926543~~ van Heerde et al. USP 6,150,081. These gelatins are referred therein as COLIA1-2 and COLIA1-1, respectively, and they are produced by transforming *Pichia pastoris* with mouse COLIA1-1 gene and expressing the gene by fermentation of the transformant *Pichia* strain.

*Please replace the paragraph at page 19, lines 19-23, with the following amended paragraph:*

The polar gelatin module (P monomer) was constructed as described in ~~previous patent applications~~ van Heerde et al. USP 6,150,081, where it is used in base emulsion applications [3]. The gene was designed to have the codon usage of *Pichia pastoris* highly expressed

genes (Sreekrishna and Kropp [4]). Two separate PCR reactions were performed, using the following oligonucleotides: